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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/737,536

12/13/2000

Daniel M. Bartell

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08/24/2006

AFFYMETRIX, INC

ATTN: CHIEF IP COUNSEL, LEGAL DEPT.

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SANTA CLARA, CA 95051

EXAMINER

WHALEY, PABLO S

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 08/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/737,536

Applicant(s)

BARTELL ET AL.

Examiner

Pablo Whaley

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 July 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-52 is/are pending in the application.
- 4a) Of the above claim(s) 32-52 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

REQUEST FOR CONTINUED EXAMINATION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/12/2006 has been entered.

CLAIMS UNDER EXAMINATION

Claims herein under examination are Claims 1-31. Claims 32-52 are again withdrawn. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

CLAIM REJECTIONS - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Applicant's arguments, filed 07/12/2006, that the instant claims are directed to a process that produces a concrete, tangible, and useful result in the microarray and biotechnology fields are not deemed to be persuasive for the reasons set forth below.

Claims 1-20 are rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter. Claims 1-9 are generally directed to a method for comparing microarray spots, which do not recite either a physical transformation of matter nor a practical application [i.e. concrete, tangible, and useful result]. Instant claim 1 recites steps drawn to providing intensity values, calculating p values, and indicating a difference if p values are greater than a significance level. As the Specification does not provide limiting definitions such that these steps are necessarily physical steps, the claim does not result in a physical transformation of matter. Where a claimed method does not result in a physical transformation of matter, it may be statutory where it recites a concrete, tangible, and useful result (i.e. a practical application). However, no actual, concrete result is recited in the claims, nor is any useful result "produced" in a tangible form useful to one skilled in the art.

Claims 10-20 are directed to a computer software product for comparing a first microarray spot A with a second microarray spot B. Computer program code which is not structurally and functionally interrelated to some physical element is considered non-functional descriptive material, which is not statutory. For the reasons set forth above, the claims are not

Art Unit: 1631

statutory. For an updated discussion of statutory considerations with regard to non-functional descriptive material and computer-related inventions, see the Guidelines for Patent Eligible Subject Matter at 1300 OG 142, Annex IV, Nov. 22, 2005.

CLAIM REJECTIONS - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 10, and 21 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Claims 1, 10, and 21 recites steps directed providing intensity values, calculating p values using a Wilcoxon rank test, and indicating a difference if p values are greater than a significance level. As the use of any type of "Wilcoxon rank test" for p-value calculation typically requires the computation of the "rank-sums" for the data points (i.e. a rank-sum statistic), however there is no step directed to "ranking" or "summing" of the data recited in the instant claims. It is noted that instant claims 9 recites "combining" intensity values, however this occurs if the said p-value is greater than a significance level. Clarification is requested.

Claims 1-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 10, and 21 recite "comparing a first microarray spot A with a second microarray spot" in the preamble. However, as the instant claims do not recite any steps directed to "comparing", it is unclear in what way the instant steps of the instant claims achieve

Art Unit: 1631

the purpose of the preamble. Clarification is requested. Furthermore, it is unclear whether spot A and spot B are provided from the same microarray, or if there are two distinct microarrays, wherein spot A refers to a first microarray and spot B refers to a second microarray. Clarification is requested.

Claims 1, 10, and 21 recite the limitation "Wilcoxon's rank test." Wilcoxon statistical tests are well known in the art, as the applicant has not specified which type of Wilcoxon statistical test is intended for the instantly claimed method (e.g. signed-rank, one-sample, two-sample, rank-sum, etc.) it is unclear as to the metes and bounds intended by applicant for the claimed "Wilcoxon's rank test" such that one skilled in the art would know which test to use. Clarification is requested. For purposes of prior art, the examiner has interpreted "Wilcoxon's rank test" to be "Wilcoxon's rank sum test" as the specification provides support for this limitation [p.32].

Claims 1, 10, and 21 recite the limitation "first microarray spot" and "second microarray spot." There is lack of antecedent basis for these limitations. Correction is requested. It is noted that claim 1 previously recites "microarray spot A" and "microarray spot B."

Claims 1, 10, and 21 recite the limitation "intensity difference between said plurality and said second plurality" (claims 1 and 10, line 9). There is lack of antecedent basis for "said plurality and said second plurality." Therefore, it is unclear as to what the said pluralities are referring to. Correction is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C.102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following prior art publications are the basis for executing this rejection:

Claims 1-8 are rejected under 35 USC § 102(b) as being anticipated by Chen et al. (Journal of Biomedical Optics, 1997, Vol. 2, No. 4, p.364-374).

Applicant's arguments, filed 07/12/2006, have been considered but are moot in view of the new ground(s) of rejection.

Chen et al. teach methods for the quantitative analysis of gene expression data using statistical tests [Abstract]. More specifically, Chen et al. teach the following aspects of the instantly claimed invention:

- A plurality of 1368 spots [p.372, Col. 2, ¶ 1] corresponding to intensity values at specific positions on a cDNA microarray substrate [Fig. 2], as in instant claims 1 and 4-8.
- Comparison of red and green signals (i.e. spots A and B) at kth gene expression levels [p.372, Col. 1, ¶ 1]

Art Unit: 1631

- A pixel selection method comprising the determination of confidence levels with intensity measurements (i.e. p-values) for two sets of independent samples (i.e. spot A and spot B), and the calculation of a rank-sum test statistics is used to test the null hypothesis.
- Calculation of a rank-sum tests statistic (W) based on average different [Equation 1] to test the null hypothesis versus an alternative hypothesis; rejection occurs when W is \geq to a critical value corresponding to the significance value α [p.368, Col. 1, ¶ 2 and 3], which is implicitly a teaching for a p-value as in instant claim 1.
- Indication of comparison results at different significance values [Fig. 4 (a) and (b)], as in instant claim 1.
- Median intensities are used as average intensity values [p.366, Col. 2, ¶ 2], which is a teaching for instant claim 2.
- Significance levels of 0.05 [Fig. 4], as in instant claim 3.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Art Unit: 1631

Claims 9-21 are rejected under 35 U.S.C. 103(a) as being made obvious by Chen et al. (Journal of Biomedical Optics, 1997, Vol. 2, No. 4, p.364-374), as applied to claims 1-8, above, in view of Statistics 240 (Statistics 240 Notes, part 4, website: www.stat.berkeley.edu/~stark/Teach/S240/Notes/ch4.htm, Copyright 1997, p.1-11) and Lemkin et al. (Nucleic Acid Research, 2000, Vol. 28, No. 22, p.4452-4459)

Chen et al. teach methods for the quantitative analysis of gene expression data using statistical tests [Abstract], as set forth above.

Chen et al. do not specifically teach a computer software product or system, as in instant claims 10-31.

Statistics 240 teaches computer code and programs for statistical analysis of data. More specifically, Statistics 240 teaches the Wilcoxon Rank-Sum Test for determining p-values and comparing data [p.2] and MatLab code [p.5-6], as in instant claims 10-20.

Lemkin et al. teach a data analysis system and program (MAExplorer) for analyzing spots of gene expression data. Numeric values of expression data for each spot on the microarray are obtained [Fig. 2], and several user specified statistical methods are disclosed for comparing data from different arrays [p.4455, Col. 1, ¶ 4]. As MAExplorer is used as a stand-alone program or with a user's web browser, it inherently contains a processor and memory for causing a computer to function as a search apparatus for carrying out the above methods, as in instant claims 21-31. Lemkin et al. also teach hybridization using oligonucleotides [p.4454, Col. 2, ¶ 3], as in instant claim 9.

Thus it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to use the Wilcoxon Rank-Sum program taught by Statistics 240 and the data analysis system of Lemkin et al. with the quantitative analysis method taught by Chen et al.,

Art Unit: 1631

where the motivation would have been to incorporate new statistical analysis tools to overcome difficulties arising from conventional methods for imaging in the presence of weak hybridization signals [Chen et al., p.368, Col. 1, ¶ 1]. One of ordinary skill in the art would have had a reasonable expectation of successfully combining the Wilcoxon Rank-Sum program taught by Statistics 240 and the data analysis system of Lemkin et al. as both teach computer programs for statistical analysis of data. Furthermore, both Lemkin et al. and Chen et al. specifically teach statistical analysis of microarray spot intensity data.

Art Unit: 1631

CONCLUSION

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pablo S. Whaley

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Lee A. Claw
Patent Examiner
8/18/06